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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/487,558	01/19/2000	Robert Busby	109272.130	3300

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EXAMINER
LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
1636	32

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/487,558	Applicant(s) BUSBY ET AL.	
	Examiner David A. Lambertson	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2003* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *104-224* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *104-224* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 13, 2003 (Paper No. 31) has been entered.

Claims 104-224 are pending and under consideration in the instant application. Amendments were made to the claims. Specifically, the claims have been more narrowly defined than in the previous claims, claiming the production of more specific secondary metabolites by modifying a more narrow range of gene products.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 104-109, 113, 119,144-148, 150-153, 156, 157 and 160, drawn to a method for modulating the production of a secondary metabolite, specifically a polyketide, by over-expressing a gene in a fungus, classified in class 435, subclass 41.

II. Claims 104-108, 110, 113, 119,144-148, 150-153, 156, 157 and 161, drawn to a method for modulating the production of a secondary metabolite, specifically a polyketide, by conditionally expressing a gene in a fungus, classified in class 435, subclass 41.

III. Claims 104-108, 111, 113, 119,144-148, 150-153, 156, 157, and 162, drawn to a method for modulating the production of a secondary metabolite, specifically a polyketide, by using a dominant negative mutation of a gene, in a fungus classified in class 435, subclass 41.

IV. Claims 104-108, 112, 113, 119,144-148, 150-153, 156, 157, and 163 drawn to a method for modulating the production of a secondary metabolite, specifically a polyketide, by using a dominant positive mutation of a gene in a fungus, classified in class 435, subclass 41.

V. Claims 104-108, 113, 119,144-148, 150-153, 156, 157 and 164, drawn to a method for modulating the production of a secondary metabolite, specifically a polyketide, by using a dominant neomorphic mutation of a gene in a fungus, classified in class 435, subclass 41.

VI. Claims 120-125, 131-137, 143, 168-177, 198-207, 211 and 216-221, drawn to a method for providing a fungal cell for secondary metabolite production by transforming the fungal cell with an overexpressed gene, and the resulting cells, classified in class 435, subclass 254.1.

VII. Claims 120-125, 131-137, 143, 168-177, 198-207, 212 and 216-221, drawn to a method for providing a fungal cell for secondary metabolite production by transforming the fungal cell with a conditionally expressed gene, and the resulting cells, classified in class 435, subclass 254.1.

VIII. Claims 120-125, 131-137, 143, 168-177, 198-207, 208and 216-221, drawn to a method for providing a fungal cell for secondary metabolite production by

transforming the fungal cell with a dominant negative mutant gene, and the resulting cells, classified in class 435, subclass 254.1.

IX. Claims 120-125, 131-137, 143, 168-177, 198-207, 209 and 216-221, drawn to a method for providing a fungal cell for secondary metabolite production by transforming the fungal cell with a dominant positive mutant gene, and the resulting cells, classified in class 435, subclass 254.1.

X. Claims 120-125, 131-137, 143, 168-177, 198-207, 210 and 216-221, drawn to a method for providing a fungal cell for secondary metabolite production by transforming the fungal cell with a dominant neomorphic gene, and the resulting cells, classified in class 435, subclass 254.1.

XI. Claims 150-154, 159, 160, 181-183, 187, 188, 190, 194, 195, 222 and 223, drawn to a method of modulating the production of a secondary metabolite, specifically a β-lactam, by over-expressing a gene in a fungus, classified in class 435, subclass 43.

XII. Claims 150-154, 159, 161, 181-183, 187, 189, 190, 194, 195, 222 and 223, drawn to a method of modulating the production of a secondary metabolite, specifically a β-lactam, by conditionally expressing a gene in a fungus, classified in class 435, subclass 43.

XIII. Claims 150-154, 159, 162, 181-183, 187, 184, 190, 194, 195, 222 and 223, drawn to a method of modulating the production of a secondary metabolite, specifically a β-lactam, by using a dominant negative mutation of a gene in a fungus, classified in class 435, subclass 43.

XIV. Claims 150-154, 159, 163, 181-183, 187, 185, 190, 194, 195, 222 and 223, drawn to a method of modulating the production of a secondary metabolite, specifically a β-lactam, by using a dominant positive mutation of a gene in a fungus, classified in class 435, subclass 43.

XV. Claims 150-154, 159, 164, 181-183, 187, 186, 190, 194, 195, 222 and 223, drawn to a method of modulating the production of a secondary metabolite, specifically a β-lactam, by using a dominant neomorphic mutation of a gene in a fungus, classified in class 435, subclass 43.

XVI. Claim 149, drawn to a polyketide, classified in class 514, subclass 1.

XVII. Claim 224, drawn to a β-lactam, classified in class 514, subclass 192.

Concerning claims 104, 108, 120, 124,, 132, 136, 150, 159, 168, 177, 181, 187, 196, 197, 206, and 207, they are claimed in a Markush type format; however the members of the group do not possess unity of invention and instead are patentably distinct inventions recited in the alternative. The members of the group are different and patentably distinct from each other because each member is a different a different gene, each having a distinct biochemical sequence, structure and biochemical function, therefore there is no functional relationship between the members of the group (See MPEP 803.02). Upon election of any Group that contains any of the aforementioned claims, Applicant is required to elect one (1) of the members of the group set forth in the claim. This is NOT an election of species because there is no linking biochemical function for each of the genes recited in the Markush group.

Specifically, for applicant's ease in determining which claims should be elected with each group when considering the individual genes, the election of the following genes in the following groups will add the corresponding claims to the elected group:

1. Concerning groups I-V, election of : ganB adds claim 114, gpa3 adds claim 115, creA adds claims 116 and 165, lys14 adds claim 117, Pc23 adds claim 118, pacC adds claim 167 and lovE adds claim 166.

2. Concerning groups VI-X, election of: ganB adds claims 126 and 138, gpa3 adds claims 127 and 139, creA adds claims 128, 140, 178, 198 and 213, lys14 adds claims 129 and 141, Pc23 adds claims 130 and 142, pacC adds claim 180, AAD34561 adds claims 200 and 215 and lovE adds claims 179, 199 and 214.

3. Concerning groups XI-XV, election of: creA adds claims 165 and 191, lovE adds claims 166 and 192 and AAD34561 adds claim 193.

A proper response to this restriction requirement must include the election of a corresponding gene, otherwise the response will be considered non-responsive.

Claim 150 link(s) the inventions of Groups I-V and XI-XV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 150. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional

application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct, each from the other because of the following reasons:

Inventions I-V are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions and modes of operation and are not disclosed as capable of being used together. Specifically, groups I-V use different genetic manipulations in order to produce the polyketide by the claimed method. Over-expressing a gene (I) requires different method steps than conditionally expressing a gene (II). Similarly, there is no need to overexpress or conditionally express dominant mutations (III-V), as the functions of these mutations are a property of the mutation itself, and not the effect of the level of expression of the protein. Furthermore, the functions of each type of mutant/expression level are different because each manipulation confers a distinct property on the gene (e.g., it is overproduced, produced selectively or it has an inactivating mutation). Because these methods use different modes of operation and have different functions, the methods are patentably distinct.

Inventions VI-X are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions and are not disclosed as capable of being used together. Specifically, groups VI-X comprise different genetic manipulations in order to produce the claimed fungal cells. A cell that overexpresses a gene is not equivalent to a cell that expresses a dominant mutation, nor is it equivalent to a cell that conditionally expresses a gene. For example, overexpression requires that a gene be expressed at levels higher than the normal level as contained in a cell, whereas conditional expression requires that the gene only be expressed under certain conditions. Furthermore, dominant mutations can be expressed at the normal level of the protein in order to exert an effect, therefore there is not necessarily a need to overexpress or conditionally express such genes. As a result, cells that overexpress, conditionally express, or comprise dominant negative, dominant positive or dominant neomorphic mutations are patentably distinct because the cells have different functions.

Inventions XI-XV are unrelated to each other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions and modes of operation and are not disclosed as capable of being used together. Specifically, groups XI-XV use different genetic manipulations in order to produce the β-lactam by the claimed method. Over-expressing a gene (XI) requires different method steps than conditionally expressing a gene (XII). Similarly, there is no need to

overexpress or conditionally express dominant mutations (XIII-XV), as the functions of these mutations are a property of the mutation itself, and not the effect of the level of expression of the protein. Furthermore, the functions of each type of mutant/expression level are different because each manipulation confers a distinct property on the gene (e.g., it is overproduced, produced selectively or it has an inactivating mutation). Because these methods use different modes of operation and have different functions, the methods are patentably distinct.

Inventions I-V and XI-XV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different effects and modes of operation and are not disclosed as capable of being used together. Specifically, one group of methods is designed to produce a polyketide (I-V) and the other group of methods is designed to produce a β-lactam (XI-XV), therefore the outcomes of each group of methods are distinct. Furthermore, these products are chemically distinct from one and other, and involve the manipulation of different metabolic pathways/genes in order to produce them, therefore the methods themselves are distinct. Because these methods each have different modes of operation and effects, they are patentably distinct from each other.

Inventions I-V and XI-XV and VI-X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that

product (MPEP § 806.05(h)). In the instant case the products (VI-X) can be used in a materially different process. For example, a cell over-expressing a particular gene can be used for the recombinant isolation of the protein, or a cell expressing a dominant negative mutation can be used in a suppression screen to identify proteins related to the biochemical pathway in which the gene participates.

Inventions XVI and XVII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different functions and are not capable as being used together. A β-lactam and a polyketide are structurally distinct chemicals with different functions (in the case of specific examples of each recited in the instant application, the β-lactam, penicillin, is an antimicrobial whereas the polyketide, lovastatin, is a regulator of sterol synthesis). Because these molecules have different functions, they are patentably distinct.

Inventions I-XV and inventions XVI-XVII are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product can be produced (and isolated) from a number of different sources, including organisms that have not undergone metabolic engineering (such as the unmodified organisms of the instant invention).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, especially in instances where the classifications are the same, the non-patent literature searches required for each of these inventions are not co-extensive, hence said searches would be burdensome. Therefore restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
March 21, 2003

Gerald D. Leffers Jr
PATENT EXAMINER
Gerald G. Leffers Jr
A.U. 1636